PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rule 72.2)

To:

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RECEIVED
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I.P. DEPT
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Date of mailing *(day/month/year)* 30 June 2005 (30.06.2005)	
Applicant's or agent's file reference 1504	**IMPORTANT NOTIFICATION**
International application No. PCT/IB2003/003470	International filing date *(day/month/year)* 22 August 2003 (22.08.2003)
Applicant KYOWA HAKKO KOGYO CO., LTD. et al	

1. **Transmittal of the translation to the applicant.**

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

2. **Transmittal of the copy of the translation to the elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

AZ, CA, CH, CN, EP, GH, KG, KR, MK, MZ, RO, RU, TM

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, BA, BB, BG, BR, BY, BZ, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, ES, FI, GB, GD, GE, GM, HR, HU, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PG, PH, PL, PT, SC, SD, SE, SG, SK, SL, SY, TJ, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

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Translation

PCT/IB2003/003470

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1504	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/IB2003/003470	International filing date (*day/month/year*) 22 August 2003 (22.08.2003)	Priority date (*day/month/year*) 22 August 2002 (22.08.2002)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 31/519, 31/55, 31/7088, 38/17, 39/395, 48/00, A61P 11/06, 43/00, C07D 401/14, 403/06, 417/14, 471/04, 519/00		
Applicant KYOWA HAKKO KOGYO CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☒ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) 1 diskette, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19 March 2004 (19.03.2004)	11 August 2004 (11.08.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2003/003470

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purpose of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

** If item 4 in Box No. I applies, the listing and /or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 9, 11-13

because:

☒ the said international application, or the said claims Nos. 9, 11-13 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See supplemental sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 9, 11-13.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of III. 1.

The inventions set forth in claims 9 and 11 to 13 pertain to methods for treatment of the human body by therapy. (PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv))

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   See supplemental sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. _____ .

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV. 3.

The technical feature common to the inventions set forth in claims 1-3 and 14-16 is prevention and/or treatment of asthma wherein an active ingredient is a substance which suppresses signal transduction-related functions of a protein having the amino acid sequence represented by SEQ ID NO: 11. The technical feature common to the inventions set forth in claims 4-8 and 10, on the other hand, is prevention and/or treatment of asthma wherein an active ingredient is a compound represented by formula (I) in claim 4.

When these two groups of inventions are compared, the technical feature common to both groups is prevention and/or treatment of asthma; however, this feature is recognized within the art (see for example WO 02/061087 A2) and, therefore, cannot be a special technical feature; therefore, the two groups of inventions cannot be said to be so linked as to form a single general inventive concept.

It should be noted that no international search report has been prepared for the inventions set forth in claims 9 and 11-13. Therefore, these are not mentioned as inventions in 1(i) and (ii) above.

V. **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	2, 4-8, 10, 15	YES
	Claims	1, 3, 14, 16	NO
Inventive step (IS)	Claims	4-8, 10	YES
	Claims	1-3, 14-16	NO
Industrial applicability (IA)	Claims	1-8, 10, 14-16	YES
	Claims		NO

2. Citations and explanations

This opinion is expressed with reference to the disclosures in the following documents, cited in the international search report.

Document 1: WO 02/061087 A2 (Lifespan Biosciences, Inc.)
Document 2: WO 00/22129 A1 (Arena Pharmaceuticals, Inc.)
Document 3: M. Heiber *et al.*, DNA Cell Biol., 1995, 14 (1), pp. 25-35
Document 4: M. S. Mahadevan *et al.*, Genomics, 1995, 30, pp. 84-88
Document 5: K. Zhu *et al.*, J. Biol. Chem., 2001, 276 (44), pp. 41325-41335
Document 6: EP 549352 A2 (Kyowa Hakko Kogyo Co., Ltd.)
Document 7: EP 325755 A1 (Kyowa Hakko Kogyo Co., Ltd.)
Document 8: JP 9-40662 A (Kyowa Hakko Kogyo Co., Ltd.)
Document 9: Y. Nishiya *et al.*, Biol. Pharm. Bull., 2001, 24 (6), pp. 628-633

Claims 1, 13, 14, 16

Document 1, in the claims, paragraphs [265] and [266] of the description and SEQ ID NO: 272 and 273 and 1321 to 1324, discloses amino acid sequences for GPR4 and nucleotide sequences for genes coding the same; it also indicates that antibodies constructed using peptides and

oligonucleotides possessing only parts of these sequences, and specifically partial peptides of GPR4 having an amino acid sequence represented by SEQ ID NO: 1321 to 1324 and oligonucleotides coding the same, are useful in the management of asthma.

Therefore, the inventions set forth in claims 1, 13, 14 and 16 are not novel and do not involve an inventive step in the light of the disclosure in document 1.

Claims 2 and 15

The inventions set forth in claims 2 and 15 differ from document 1 in as much as an oligonucleotide having a nucleotide sequence complementary to part of the gene coding GLR4 is the active ingredient. However, construction of an oligonucleotide having a nucleotide sequence complementary to part of the gene coding a protein having a specified function, and use thereof as an active ingredient in order to suppress the protein in question, is conventional practice in the art, and a person skilled in the art would not require creative skill in order to investigate this in the case of GLR4.

Therefore, the inventions set forth in claims 2 and 15 do not involve an inventive step in the light of document 1.

Claims 4-8 and 10

The inventions set forth in claims 4 to 8 and 10 differ from document 1 in that the active ingredient is represented by formula (I).

In this connection, documents 2 to 5 all disclose facts relating to the function and/or sequence of GPR4, but do not mention in their contents anything relating to the active ingredient in these claims. Similarly, documents 6 to 9 disclose the possible pharmaceutical use of compounds having a structure analogous with compounds

set forth in these claims, but all of these differ in substituent groups or the structure of the condensed ring moiety, and do not share the same function of target disorder. Given this, it cannot ve said that a person skilled in the art could easily deduce the inventions set forth in these claims.

Therefore, the inventions set forth in claims 4 to 8 and 10 involve an inventive step relative to documents 1 to 9.